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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/846,346	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 36-43* is/are pending in the application.

4a) Of the above claim(s) *1 and 41-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1 and 36-43* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 6/16/03 is acknowledged and has been entered. Claim 1 has been amended. Claims 2-35 have been cancelled. Claims 36-43 have been added. Accordingly, claims 1 and 36-43 are pending.

Newly submitted claims 41-43 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 41-43 are drawn to a diagnostic kit that includes thereto, an antibody that binds to a specific peptide in order to provide a diagnosis of Type II diabetes.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 1 and 41-43 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Accordingly, claims 1 and 36-43 are pending. Claims 36-40 are under examination.

Rejections Withdrawn

2. The rejections of claims 3-28 are now moot in light of Applicant's cancellation of the claims.

3. In light of Applicant's amendment, the rejection of claims 36-40 under 35 U.S.C. 103(a) as being unpatentable over Hutchens et al. (US 6,225,047) in view of

Capiaumont et al. (Assay of seric human hexapeptide (HWESAS) using a monoclonal antibody and ELISA, Clinica Chimica Acta 293: 89-103 (2000)), is hereby, withdrawn.

Specification

4. The amendment filed 6/23/03 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the disease specific marker consisting of amino acid residues 2-17 of SEQ ID NO: 1. See page 27, last full paragraph and brief description of Figure 1.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 36-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36, step b) is non-idiomatic and, therefore, ambiguous in reciting, "elucidation of discernible peptides" because it is unclear what Applicant intends to encompass in reciting the terms, "elucidation" and "discernible" as used in the claim.

Perhaps Applicant intends, "[maximize] spectral analysis of peptide fragments obtained or contained therein".

Claim 36, step c) is non-idiomatic and, therefore, ambiguous in reciting, "peptides elucidated" because it is unclear what Applicant intends to encompass in reciting the terms, "elucidated" as used in the claim. Perhaps Applicant intends, "peptides obtained and analyzed from the sample".

Claim 36, step c) is vague and indefinite in failing to recite a positive limitation in the claim in reciting, "wherein recognition of a mass spectrum profile in the sample ... is diagnostic for Type II diabetes". Perhaps, Applicant intends, "wherein a mass spectrum profile in the sample ... is diagnostic for Type II diabetes."

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 36-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide literal or adequate descriptive support for the recitation of "disease specific marker consisting of amino acid

residues 2-17 of SEQ ID NO: 1". Applicant's disclosure at page 27, last full paragraph, only provides that the disease specific marker has a sequence identified as SEQ ID NO: 1, but no specific reference to amino acid residues 2-17 is set forth. Likewise, the brief description of Figures 1 and 2 in the specification, only provides that the disease specific marker has a particular sequence showing SEQ ID NO: 1, but also fails to provide literal support for the recitation of "disease specific marker consisting of amino acid residues 2-17 of SEQ ID NO: 1". Additionally, none of the originally filed claims recited the limitation in question. Recitation of claim limitation lacking literal support in the specification or originally filed claims constitutes new matter.

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 36-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the

invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method for diagnosing Type II diabetes by obtaining a sample from a patient, subjecting the sample to mass spectrometric analysis to obtain and identify peptide fragments, and comparing the mass spectrum profile of the sample with the mass spectrum profile of a peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1, wherein a display by the sample of a characteristic mass spectrum profile of a peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1, is diagnostic for Type II diabetes.

The state of the prior art- the prior art of record fails to disclose a method for diagnosing Type II diabetes by obtaining a sample from a patient, subjecting the sample to mass spectrometric analysis to obtain and identify peptide fragments, and comparing the mass spectrum profile of the sample with the mass spectrum profile of a peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1, wherein a display by the sample of a characteristic mass spectrum profile of a peptide consisting of amino acid 2-17 of SEQ ID NO: 1, is diagnostic for Type II diabetes.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the claimed method which shows isolation and identification of a peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO: 1, specifically supports diagnosis of Type II diabetes.

The amount of direction or guidance present- the specification fails to provide guidance to enable the use of isolated and identified peptide fragments consisting of amino acid residues 2-17 of SEQ ID NO: 1, to be diagnostic or indicative specifically of Type II diabetes.

The presence or absence of working examples- there are no working examples that show data and results wherein isolation and identification of a peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO: 1, specifically supports diagnosis or indication of Type II diabetes. Figure 1 shows a limited pool of 7 Type II diabetes patients displaying the characteristic mass spectrum profile of the peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed based on the instant specification.

The relative skill of those in the art-the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to a method for diagnosing Type II diabetes by obtaining a sample from a patient, subjecting the sample to mass spectrometric analysis to obtain and identify peptide fragments, and comparing the mass spectrum profile of the sample with the mass spectrum profile of a

peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1, wherein a display by the sample of a characteristic mass spectrum profile of peptide fragments consisting of amino acid 2-17 of SEQ ID NO: 1, is diagnostic for Type II diabetes.

In page 12, lines 1-17 of the specification, Applicant generally discusses SELDI-MS and time-of-flight (TOF) detection procedures which are used to maximize the diversity of biopolymers which are verifiable within a particular sample for analysis of their ability to enable diagnosis of a disease state relative to the presence or absence of the biopolymer marker. Pages 12-16 of the specification provides numerous biopolymer markers associated with diseases of the complement system, i.e. the major effector of the humoral branch of the immune system (C3 deficiency- recurrent bacterial infection and autoimmune reactions, etc.), and the Syndrome X continuum, i.e. multifaceted syndrome (insulin resistance/hyperinsulinemia, dyslipidemia, hypertension, obesity, glucose intolerance, non-insulin dependent diabetes mellitus, etc). In page 27, line 17 to page 28, line 2, Applicant provides that a specific disease specific marker which is SEQ ID NO. 1 having a molecular weight of about 1998 daltons, characterized as a C3f fragment from the complement system, has been isolated and identified and has a characteristic profile set forth in Figure 2. Applicant points to Figure 1 and notes that from the data set forth therein, one can conclusively deduce that the marker which is SEQ ID NO. 1 provides indication of Type II diabetes. However, the data set in Figure 1 only consists of an assay pool of 7 Type II diabetes patients who exhibit the presence of the claimed marker. Nowhere in the limited disclosure provides a description of how and why the peptide fragment having SEQ ID NO. 1 is conclusively a marker diagnostic

of Type II diabetes based on its manifestation in relation to the characterization of the disease. Nowhere in the specification provides adequate description that supports the assertion that a peptide fragment consisting of amino acid 2-17 of SEQ ID NO: 1 is specifically diagnostic of Type II diabetes. There is no evidentiary showing, given the instant specification and data obtained from Figure 1, that one skilled in the art would have deduced that that the claimed peptide fragment having 17 amino acid residues is a reactive marker that is diagnostic of Type II diabetes, because a population of 7 subjects is not a significant assay pool to draw one to such conclusion. Additionally, the 7 subjects in Figure 1 from whom the samples were obtained appear to be known Type II diabetes patients; hence, there is no representation of previously unknown subjects that would have been diagnosed of having Type II diabetes using the instant peptide fragment having SEQ ID NO. 1. There are also no working examples that would lead one skilled in the art to arrive to conclusion that the peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1 in the specification is a specific diagnostic marker for Type II diabetes. Alternatively, Capiaumont et al. is prior art that teaches that a peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1 (C3f or SSKITHRIHWESASLLR), is a fragment of human complement containing HWESAS motif which exhibits an indication of chronic renal failure, and not Type II diabetes. Accordingly, there is reason to believe that the subjects from whom the samples in Figure 1 are obtained, may have a possible indication of chronic renal failure as well, or that an indication of chronic renal failure cannot be excluded from those who are

deemed to have Type II diabetes, using the instant peptide fragment having SEQ ID NO. 1.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. It has been set forth above that 1) the experimentation required to enable diagnosis of Type II diabetes using the isolation and identification of a peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO: 1, would be great as 2) there is no experimental evidence provided that would indicate that the claimed method would work to diagnose Type II diabetes, using the peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO: 1; 3) there is no adequate guidance that shows that the claimed method can be used to diagnose Type II Diabetes using the peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO: 1 that is isolated and identified, 4) the nature of the invention is a method for diagnosing Type II diabetes by obtaining a sample from a patient, subjecting the sample to mass spectrometric analysis to obtain and identify peptide fragments, and comparing the mass spectrum profile of the sample with the mass spectrum profile of a peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO: 1, wherein a display by the sample of a characteristic mass spectrum profile of a peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1, is diagnostic for Type II diabetes, 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as evidenced by the fact that no prior art has been cited that shows the claimed peptide fragment is a reactive marker specifically diagnostic or indicative of Type II diabetes, and lastly 7) the claims recite a

method for diagnosing Type II diabetes by obtaining a sample from a patient, subjecting the sample to mass spectrometric analysis to obtain and identify peptide fragments, and comparing the mass spectrum profile of the sample with the mass spectrum profile of a peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO: 1, wherein a display by the sample of a characteristic mass spectrum profile of a peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO: 1, is diagnostic for Type II diabetes.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Response to Arguments

8. Applicant's arguments filed 6/16/03 have been fully considered but they are not persuasive.

A) Applicant amended the claims so as to be limited to a specific biopolymer marker peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1 that is diagnostic of Type II diabetes. Applicant contends that each patient listed in the data table shown in Figure 1 has a history of Type II diabetes and shows the presence of the 1998 dalton marker as claimed. Applicant, thus, concludes that the claims, as currently recited, are enabled; hence, overcoming the 35 USC 112, first paragraph, rejection.

In response, Applicant's argument is not persuasive because the data set in Figure 1 only consists of a limited assay pool of 7 Type II diabetes patients who exhibit the presence of the claimed marker. There is no other evidentiary showing in the

instant specification, that one skilled in the art would have deduced that that the claimed peptide fragment having 17 amino acid residues is a reactive marker that is diagnostic of Type II diabetes, because a population of 7 subjects is not a significant assay pool to draw one to such conclusion. Additionally, the 7 subjects in Figure 1 from whom the samples were obtained are known Type II diabetes patients; therefore, there is no representation of a population of previously unknown subjects that would have been diagnosed of having Type II diabetes using the instant peptide fragment having SEQ ID NO. 1.

With regards to specificity, prior art (Capiaumont et al.) shows that the peptide consisting of amino acid residues 2-17 of SEQ ID NO: 1 (C3f or SSKITHRIHWESASLLR), which is a fragment of human complement containing HWESAS motif, also exhibits an indication of chronic renal failure. This is contrary to Applicant's deductive conclusion since an indication of chronic renal failure has been identified and equated with the claimed peptide fragment having SEQ ID NO. 1 by prior art; hence, a diagnosis of chronic renal failure cannot be excluded from those who are deemed to have Type II diabetes, using the instant peptide fragment having SEQ ID NO. 1.

Response to Declaration

9. Applicant provides a Declaration under 37 CFR 132 in order to establish the specificity of the claimed marker. According to Applicant, the profiles shown in the figure attached to the declaration indicate that the claimed method can be used to

distinguish individuals suffering from Type II diabetes from those not inflicted with Type II diabetes (normal individuals) and that the figure provides side-by-side profiles of normal human sera versus patients having Type II diabetes. Applicant then argues that the profile comparison clearly evidences the absence of the 1998 dalton marker in normal human sera and thus establishes the specificity of the 1998 dalton peptide marker which when present is diagnostic for Type II diabetes.

In response, Applicant's 1.132 declaration has low probative value in supporting Applicant's conclusion that the peptide fragment consisting of 2-18 amino acid residues of SEQ ID NO: 1 is a specific reactive diagnostic marker in a method of diagnosing Type II diabetes because the figure submitted with the declaration represents side-by-side profiles limited to a comparison between serum profile of individuals having Type II diabetes to the serum profile of non-diseased individuals. Applicant has not provided evidentiary showing that a population of previously unknown subjects can be specifically identified and diagnosed of having Type II diabetes using the claimed method and peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO. 1, which is recited in the rejected claims. Additionally, prior art (Capiaumont et al.) shows that the claimed peptide fragment is also exhibited in patients having chronic renal failure. This is contrary to Applicant's deductive conclusion that the peptide fragment consisting of amino acid residues 2-17 of SEQ ID NO. 1 is diagnostic of Type II diabetes since an indication of chronic renal failure has been identified and equated with the same claimed peptide fragment; and therefore, the peptide fragment cannot be rendered as specific only for diagnosis of Type II diabetes.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
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Art Unit 1641
August 11, 2004

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8/21/04